<u>Abstract of the Disclosure</u>

The use of enzymes which catalyze the production of starter and extender units for polyketides is described. In addition, modified loading modules are described, which can accept a variety of starting units such as substituted benzoates, and which can be used to generate substituted derivatives of natural products. These enzymes may be used to enhance the yield of polyketides that are natively produced or polyketides that are rationally designed. By using these techniques, the synthesis of a complete polyketide has been achieved in *E. coli*. Production can be enhanced in microbial organisms of polyketides and other secondary metabolites by delaying production until after exponential phase and by maintaining relatively constant nutrient levels in the medium. In addition, polyketide production can be enhanced by providing an expression system for a thioesterase II. Thus, by modifying the host organism and changing the culture conditions, synthesis of a secondary metabolite can be enhanced. The present invention also results in a host organism with desirable characteristics to be used in the production of such polyketides and to assess the results of gene shuffling.